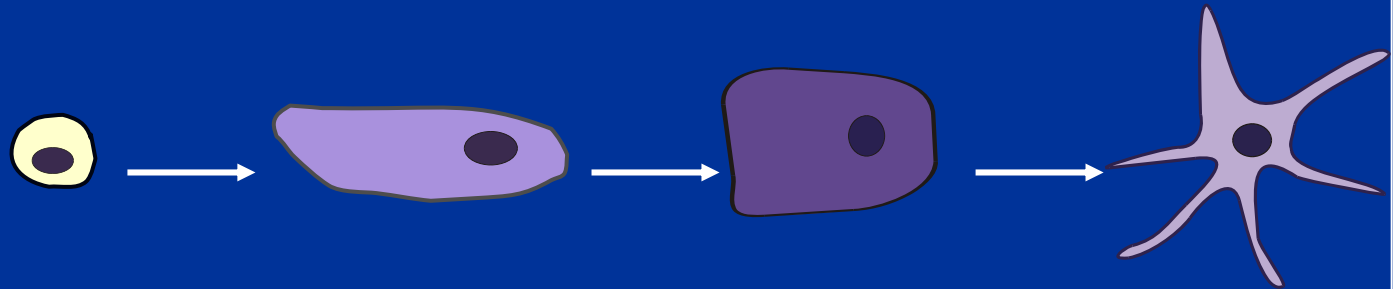


# Mesenchymal stem cells in skeletal repair

”Living implant”

# DIFFERENTIATION and Function of BONE CELLS

## Osteoblast lineage



mesenchymal  
stem cells

pre-osteoblast

osteoblast

osteocyte

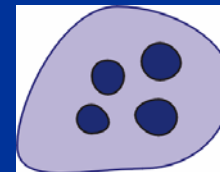
## Osteoclast lineage

hematopoietic  
stem cells

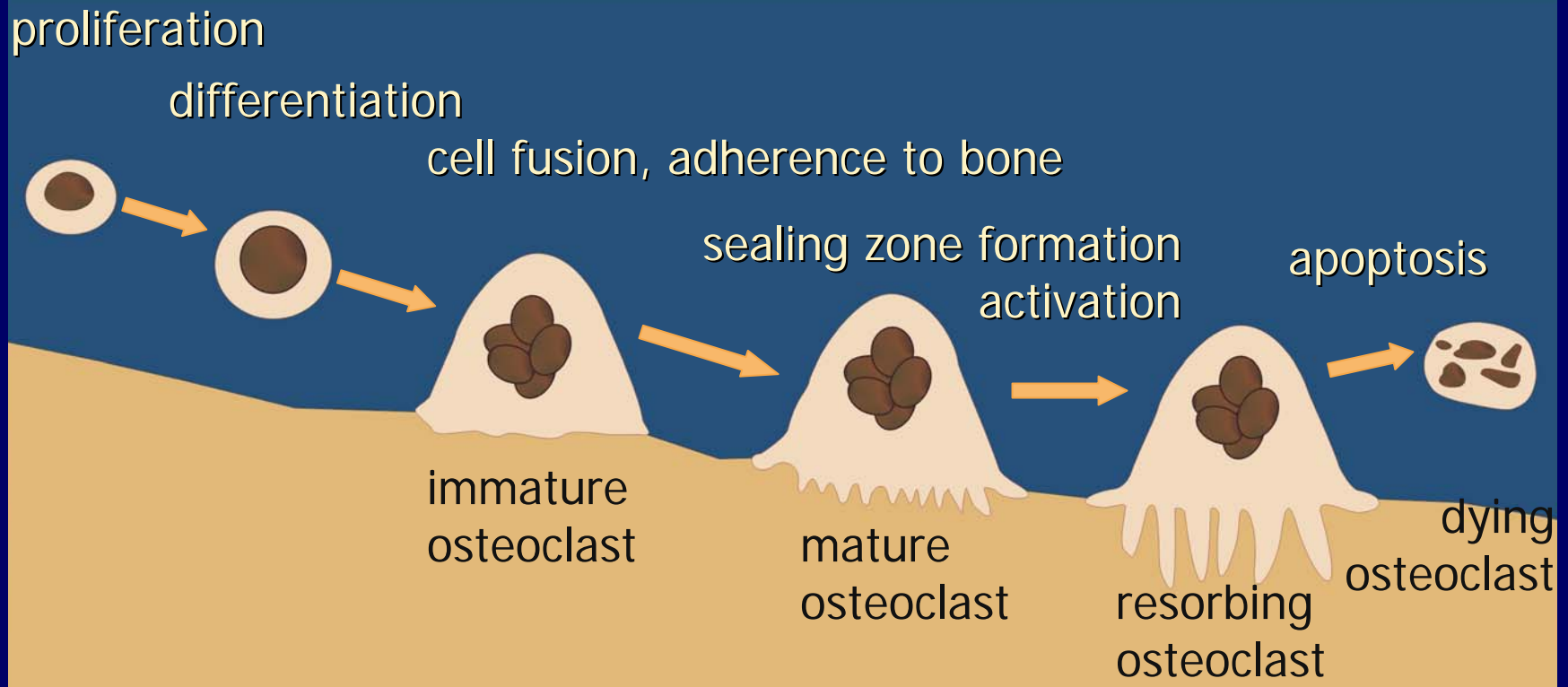
pre-osteoclast

multinucleated  
osteoclast

activated  
osteoclast

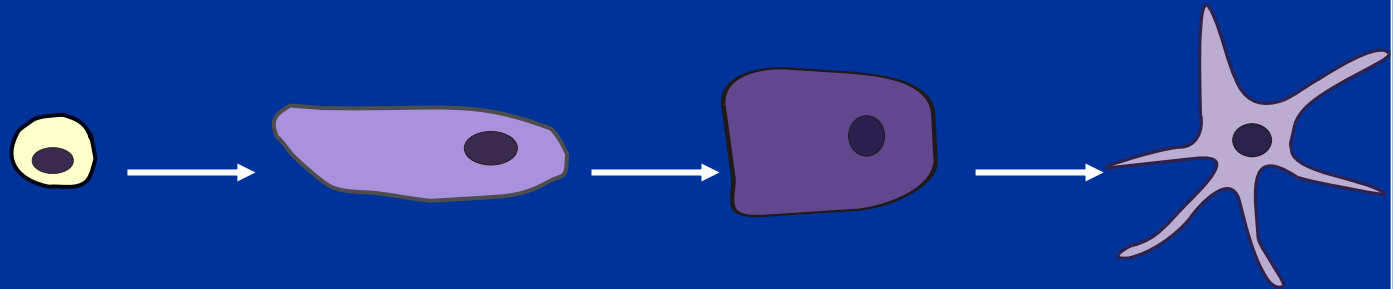


# In vitro model for osteoclast cell biology ("Pharmatest Services" and "SBA")



# DIFFERENTIATION and Function of BONE CELLS

## Osteoblast lineage



mesenchymal  
stem cells

pre-osteoblast

osteoblast

osteocyte

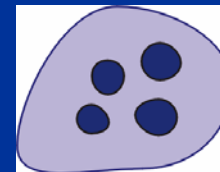
## Osteoclast lineage

hematopoietic  
stem cells

pre-osteoclast

multinucleated  
osteoclast

activated  
osteoclast



# ”Living implant- concept”

- Goal: New therapies to repair of difficult bone defects
- Strategy: Combination of suitable biomaterials and autologous adult MSCs to create ”living implants”

# Research Concoortium

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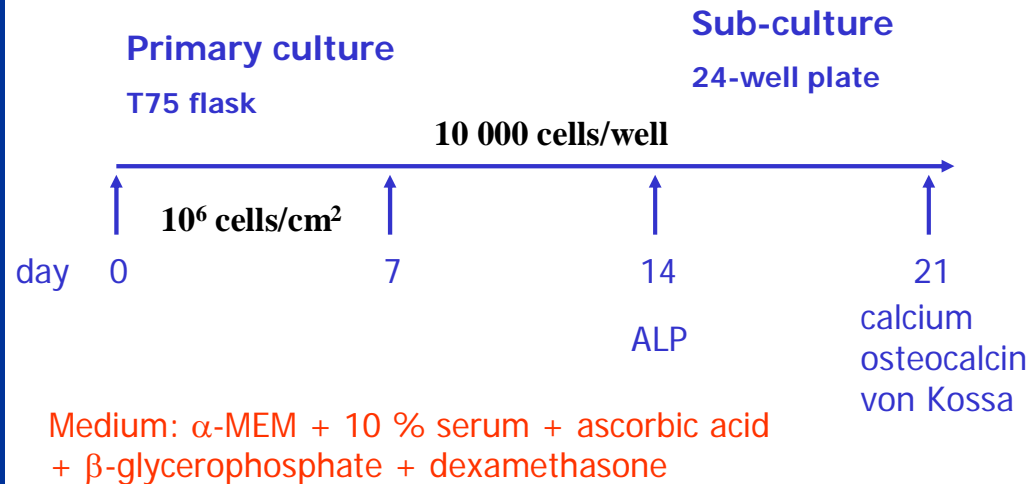
Biomaterial companies

# "Living explant-concept"

- Source of MSCs: autologous bone marrow or blood
- In vitro expansion: amount of cells, safety, optimal support material, ingrowth of cells
- Experimental in vitro "proof of concept" model
- Clinical applications

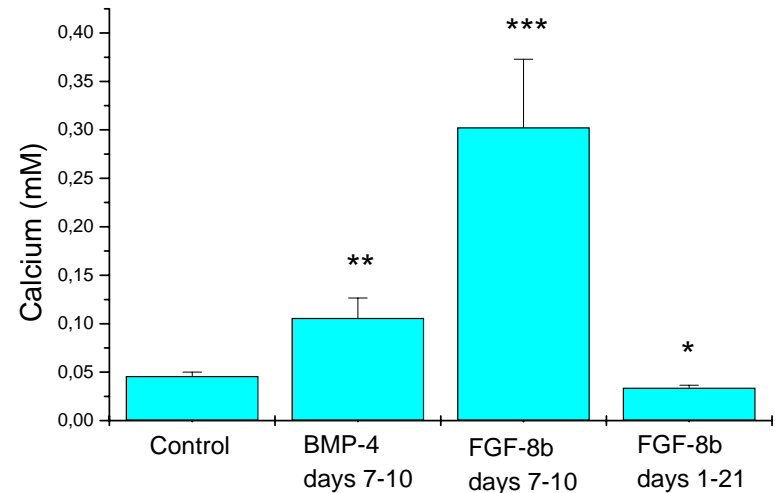
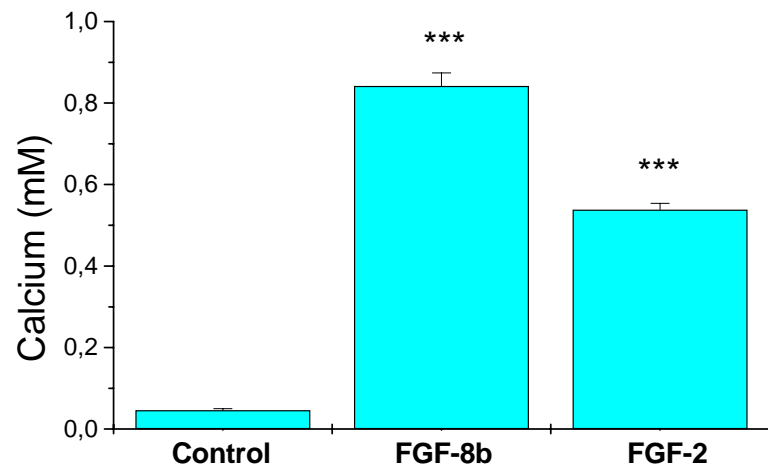
# In vitro bone formation assay a la Friedenstein (1968)

## Principle of bone formation assay

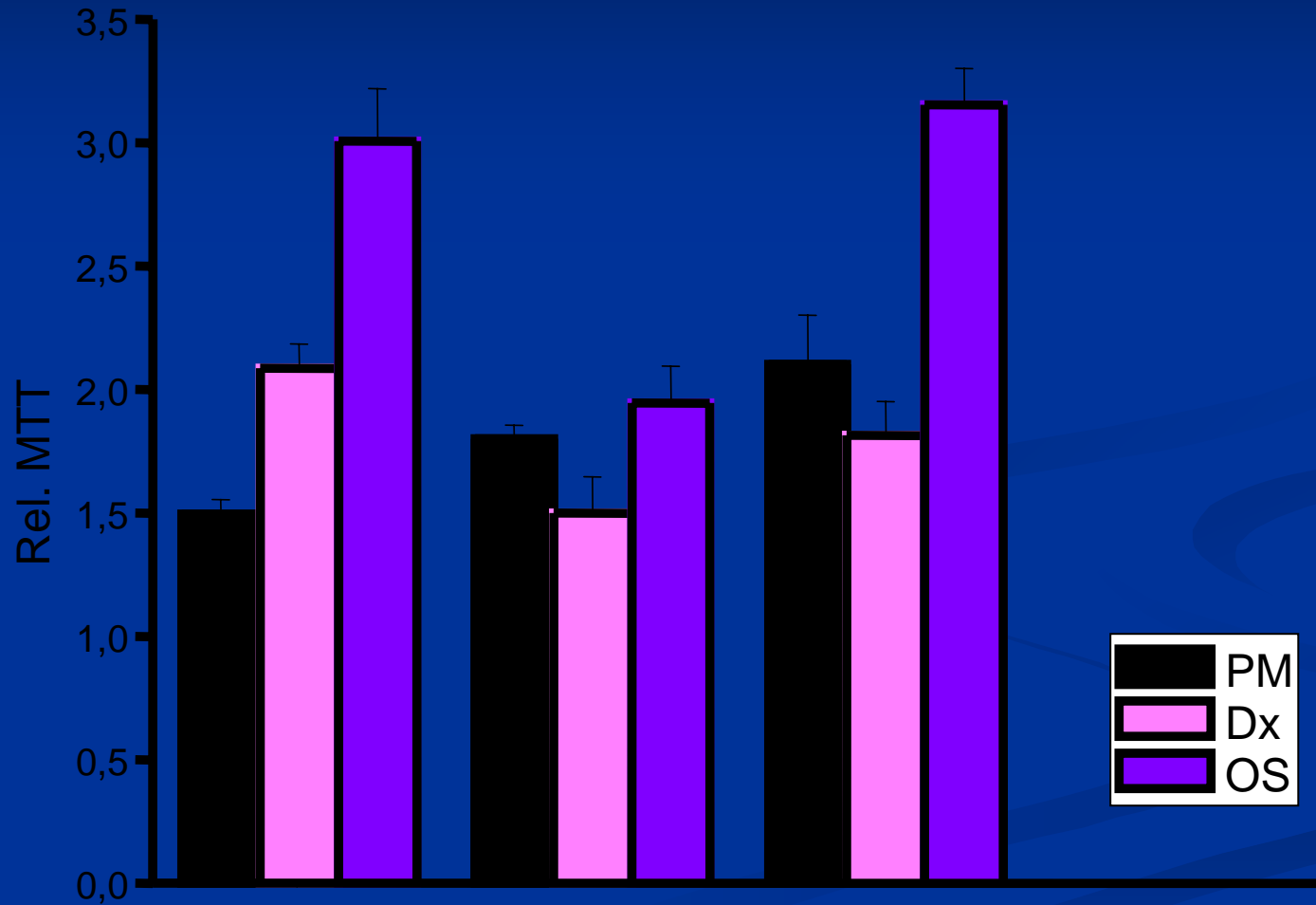




# In vitro expansion and differentiation of MSCs to bone forming cells



# hMSCs are proliferating in biomaterials



# MSC differentiation in different biomaterials in vitro



# In vivo "proof of concept"- assay



# Cell Culture Facilities Next to Operation Theatres



Harvest and culture of cells from patients

Clinical experiments where usefulness of cellular therapy could be tested

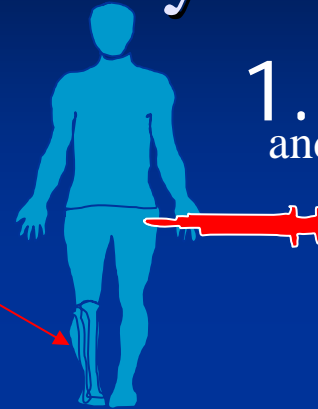
Alert of applications of cellular therapies that could be employed in every day surgical practise

# Transplantation of MSCs back into patients: principle of the preliminary clinical trial



Tibial Nonunion

20.000.000 hMSCs



1. Bone marrow is harvested from iliac crest and expansion of MSCs in cult



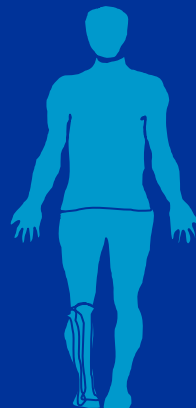
2 weeks of culture

'Live implants'



Cells in solution

2.



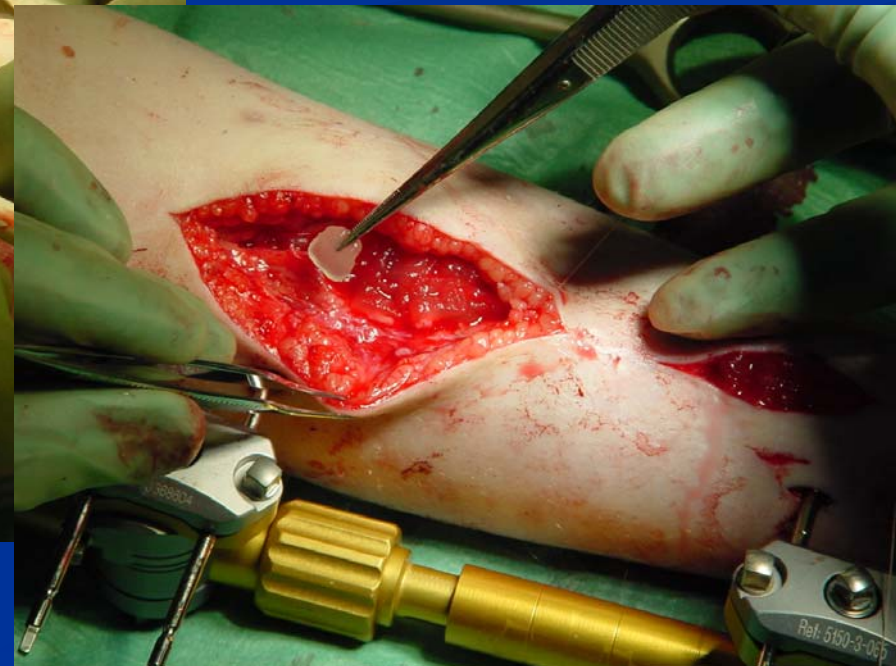
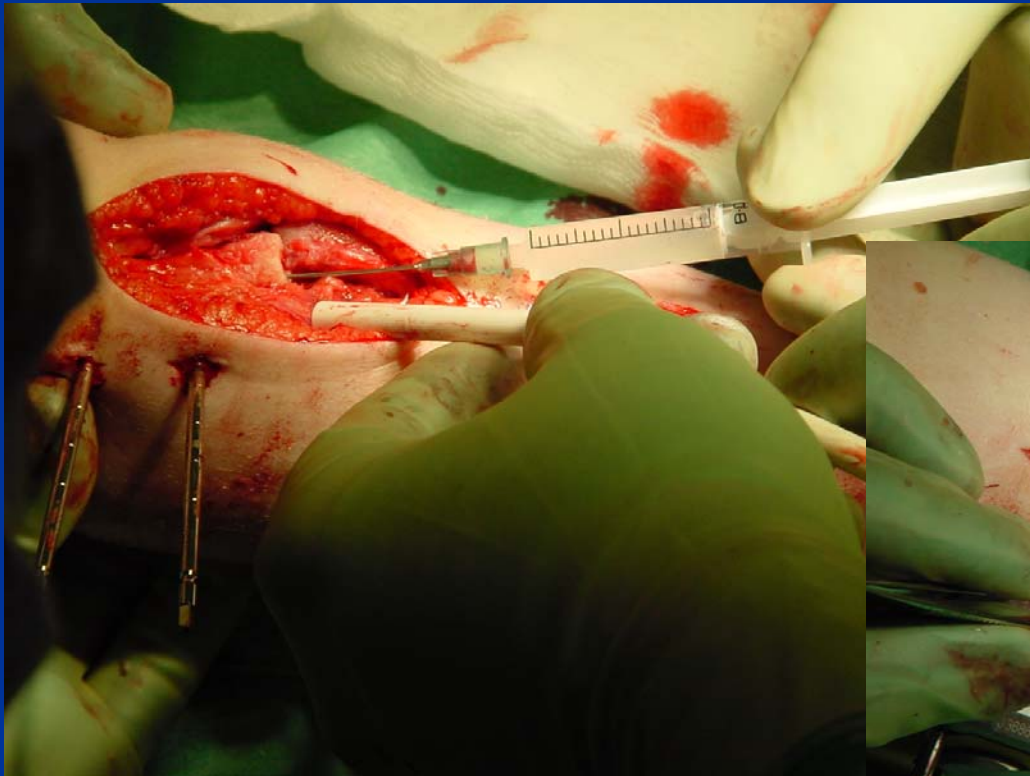
3.

Implantation of bone marrow cells into bone defect with or without carrier

Osteoinduction occurs, healing the bone defect?



# Bone repair: Cells embedded in the selected carrier



# "Living implant"

- Could be a potential solution to enhance bone fracture healing
- Use of autologous cells: 1) no ethical or immunological problems 2) expansion of MSCs remains a problem but could be solved 3) safety of expansion
- Selection of optimal biomaterial is critical
- Relevant in vivo proof of concept- experiment
- Selection of patients



# Future plans

- Optimization of expansion/differentiation continues
- Selection of optimal support material continues
- Model for experimental "proof of concept"; ok
- Preliminary aim to go into larger clinical trial  
2007/2008